June 1, 2004

For Electronic Submission

Richard Carmona, MD
United States Surgeon General
United States Department of Health and Human Services
Chairman, Task Force on Importation
Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. 2004N-0115
Request for Comment on Prescription Drug Importation

Dear Dr. Carmona and Members of the HHS Task Force on Importation:

The Biotechnology Industry Organization (BIO) submits the following comments in response to the notice published by the Food and Drug Administration (FDA) on March 18, 2004 (69 FR 12810) regarding the Department of Health and Human Services' (HHS's) Task Force on Drug Importation (the Task Force) established to study prescription drug importation as mandated by the Medicare Prescription Drug, Improvement and Modernization Act of 2003 (MMA). The MMA requires the Secretary of HHS (the Secretary) to conduct a study to explore the design of a prescription drug importation system that the Secretary may certify as (1) posing no additional risk to public health and safety and (2) resulting in a significant reduction in the cost of prescription drugs in the United States.

BIO represents more than 1,000 biotechnology companies, academic institutions, state biotechnology centers and related organizations in all 50 U.S. states. BIO members are involved in the research and development of health care, agricultural, industrial and environmental biotechnology products. BIO and its members are committed to the safety of the U.S. drug supply. We also support efforts to increase U.S. consumers' access to safe and effective prescription drugs.

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The Secretary's Task Force held a Public Meeting on April 14, 2004, at which BIO briefly presented some of its concerns. We have attached for your convenience a copy of BIO's statement presented at that meeting. *See* Exhibit A. Additionally, the Task Force seeks stakeholder input in the form of answers to eleven comprehensive multi-part questions.1 Below is our response.

COMMENTS

SCOPE AND VOLUME OF IMPORTED DRUGS

I. Assess the scope, volume and safety of unapproved drugs, including controlled substances, entering the United States via mail shipment.

In conducting the study, Congress directed the Department to take into account the distinctions between drugs that are biological products with licenses under section 351 of the Public Health Service Act (PHSA) and drugs with approved applications under subsection (b) or (j) of section 505 of the Food, Drug and Cosmetic Act (FDCA). The Task Force seeks information relating to the scope, volume and safety for importation of these differing types of products.

BIO's Response:

The MMA, and recent drug importation legislative proposals, expressly exclude "biological products" from the scope of any reimportation or importation scheme.2/ BIO agrees with Congress that an explicit exclusion is absolutely necessary for patient safety.3/ However, even if such an exclusion was drafted to appropriately capture all biological products, we are still concerned that it would not adequately prevent the importation of all biological products.

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1 *See h*ttp://www.hhs.gov/importtaskforce/task_force.html.

2/ 21 U.S.C. § 384(a)(3)(B) (citing 42 U.S.C. § 262).

3/ We take this position because biological products are particularly sensitive to conditions of manufacturing, storage, shipping, and handling. For instance, environmental changes can cause degradation of a biological product and reduce its therapeutic effect. Therefore, prohibiting importation of biological products, in particular, is critical to patient safety. Moreover, FDA places significant emphasis on the manufacturing process and facilities used to create biologics. Biologic products are often difficult to chemically characterize by analyzing the structure of the molecule, and manufacturing methods have an affect on a biological product's safety, purity, and potency. Thus, virtually any change in manufacturing has historically been considered significant and required FDA pre-approval. *See* 21 CFR 601.12.

Although current law and these proposals alike manifest an intended policy of exempting all biotechnology products from the scope of legal importation, they are not drafted appropriately to account for such products approved under 505(b) of the FDCA. For example, certain biologics, such as human growth hormone and insulin are not currently excluded and could still be imported.

Importation of unlicensed biological products from unlicensed facilities is currently illegal, yet the U.S. Food and Drug Administration (FDA) and the U.S. Bureau of Customs and Border Protection (CBP) have repeatedly documented personal shipments of biological products that pose serious risks to the individuals involved. Furthermore, consumers and FDA have obtained, through international mail and commercial courier shipments, biological products that were:

- improperly packaged;
- maintained at temperatures that hasten their degradation or completely destroy their effectiveness; and
- diluted, concentrated, or otherwise adulterated.

Consequently, any drug importation regulatory scheme must include strong enforcement to assure that the illegal importation of biological products is stopped and patients are protected from these dangerous practices.

Are there product characteristics that might be associated with lower risk when imported without going through the usual FDA approval and regulatory process? (For example, the type of product (injectable, controlled substance, etc.), country of origin of the import, Internet mail-order vs. personally transported products, manufactured in U.S. (though not approved for U.S. use) or other country, inclusion of U.S.-approved patient labeling, or characteristics of the shipping entity (e.g., pharmacy that primarily serves individuals of another nation, vs. a pharmacy set up primarily or entirely to handle drugs that will be consumed by residents of the United States).

BIO's response:

For the reasons discussed in response to the first question, BIO believes that the exclusions included in the MMA must be maintained, extended and enforced. Additionally, biotechnology products approved under the FDCA, parenteral products, all injectables not just intravenously injected drugs, products requiring refrigeration during storage and shipping, and photoreactive products should also be excluded. Furthermore, the Task Force should consider the countries of origin or countries through which imported drugs may be transshipped in determining whether importation should be permitted.

When in international trade, articles often move through different countries before export to a final destination (*i.e.*, a recipient in the U.S.). These "transshipments" generally occur through bonded warehouses. Products shipped to and stored in bonded warehouses are not destined for sale in the country through which they are shipped and, therefore, are not ordinarily "in" the domestic commerce of the country where the warehouse is located for tariff, duty, fee, and in many cases, regulatory oversight purposes. As a result, regulators in those countries focus little or no attention on these products.

Consequently, it is inappropriate to rely on other countries' laws to protect U.S. customers – the countries through which the products are shipped (including Canada and members of the European Union) have little if any ability to exert regulatory controls over those products. These issues are discussed more fully in our response to section III.

The Task Force seeks information on whether or not these imports, or some of these imports, could meet U.S. approval standards or the equivalent. What is the scope and volume of drugs commercially available in other countries that are actually FDA-approved?

BIO's response:

FDA approval has long been viewed as the international "gold standard." Therefore, we are puzzled by the phrase "U.S. approval standards *or the equivalent.*" Absent full FDA review and approval, a drug unapproved by FDA is just that – unapproved.

FDA stated just last month that the "overwhelming majority" of drugs intercepted by FDA and CBP in the international mail system are "unapproved." 4/ Therefore, if FDA-approved drugs are widely available in foreign markets, apparently they are *not* being sent to U.S. consumers attempting to fill prescriptions overseas.

Different countries impose different regulatory requirements on the domestic sale of drug products. Therefore, a drug approved in another country may not be bioequivalent to or have the same bioavailability as an FDA-approved drug –

4/ *See e.g.,* Statement of William K. Hubbard, FDA Associate Commissioner for Policy and Planning before the Subcommittee on Healthcare and the Subcommittee on International Trade, Senate Committee on Finance, at http://www.fda.gov/ola/2004/importeddrugs0427.html (Apr. 27, 2004).

even if the foreign drug contains the same active ingredient as the FDA-approved product. This is particularly true for biological products. A biological product similar to an FDA-approved version will likely be produced in a different facility even if it is made by the same manufacturer. That difference alone can produce a biological product with different biological activity or therapeutic effect.

The Task Force should also be aware that some legislative proposals would permit the legal importation of virtually any version of a drug available around the world which differs from its FDA-approved version, not merely those versions legally marketed in the countries deemed eligible to export to the U.S. Because the number of drug product variants marketed worldwide is unknown, this potential for "virtual transshipments" of foreign drug products would place an insupportable burden on the FDA.

Consequently, FDA does not adopt any other country's "approval status" for drug products and many other countries do not admit drugs based solely upon FDA-approval status. Therefore, BIO does not believe that the Task Force should consider adopting another country's approval standard as the "equivalent" of FDA approval for importation purposes.

For imported drugs that are not U.S.-approved, what approaches can be used to determine whether they are equivalent to U.S.-approved drugs?

BIO's response:

The drug approval process in the United States requires an *affirmative demonstration* of safety and effectiveness before any drug or biologic may be marketed. Innovator drugs, for example, cannot be marketed until the manufacturer has made an independent demonstration of safety and effectiveness through clinical trials. Generic drugs are shown to be safe and effective through a demonstration of "sameness" and bioequivalence to previously-approved drugs. BIO opposes any approach that would sanction a third class of drugs – those approved overseas under varying approval standards that are then brought into the U.S. as "equivalents" to FDA-approved products. Any proposal to allow broader importation of non-FDA approved products assumes that implementation of such an untested regime would be at least as reliable, consistent, comprehensive and efficacious as the FDA's current system of drug approval and regulation in assuring safety, effectiveness and product identity. If foreign companies can obtain access to the U.S. market under a less rigorous standards for entry, consumers will lose the protections of the existing system – which was established by Congress to protect those very consumers.

Should certain products be excluded from importation because of special risk concerns? What impact would limiting the number, types or categories of drugs that would be legally authorized to be imported have on the ability of the FDA and other Federal agencies to assure the safety of such products? The Task Force seeks input on how to establish risk-based criteria for any such limitations, e.g., chronic-use medicines, small-molecule drugs less sensitive to shipping conditions, medicines with wide therapeutic indices, medicines not subject to risk management or controlled-substance restrictions, medicines not prone to misuse.

BIO's response:

In addition to the exclusions in the MMA, BIO believes the following class of products should be excluded from any proposed drug importation program:

- All biotechnology-derived products, approved under either the FDCA or PHS Act, for the reasons set out in footnote 2.

- Products requiring special storage or handling requirements (*e.g.,* temperature, light conditions, careful handling, etc.). CBP inspectors may hold imported products at the border indefinitely while admissibility is pending. By the time these products reach the consumer, undue delays and improper storage conditions could affect the product's stability.

- Products requiring risk management, initial screening, and/or periodic patient monitoring programs should be prohibited. FDA and CBP have discovered during their import blitz examinations drugs that require close monitoring, or administration by a physician. Delivery of these products directly to patients without the knowledge or oversight of a physician can pose an unacceptable risk to patients.5/

- Drugs with dangerous interactions or those that are labeled with FDA mandated "black box" warnings should be prohibited.

- As discussed in response to the first question, FDA's blitz campaigns discovered imports of unlicensed biologic products that should be

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5/ *See e.g.,* Sept. 29, 2003 FDA Press Release; *Recent FDA/U.S. Customs Import Blitz Exams Continue to Reveal Potentially Dangerous Illegally Imported Drug Shipments*, at http://www.fda.gov/bbs/topics/NEWS/2003/NEW00948.html.

administered by healthcare providers, such as the influenza virus vaccine.6/ These imports are currently unlawful and should remain unlawful.

Additionally, it is important to recognize that exclusions are extremely difficult to administer. It is unlikely that FDA or CBP inspectors will be able to efficiently and effectively target shipments that contain prohibited products. Even if border inspectors could accurately target inspections, their ability to distinguish between prohibited and permitted drug products would be a costly and time consuming exercise in frustration and futility.

Restricting drug importation to a designated list of permitted drug products or categories might appear to hold promise for making a drug importation inspection regime manageable. However, CBP and FDA inspectors would still have to open each package in each shipment to ensure its contents were permitted and had undergone appropriate quality assurance testing. Certification of a drug importation program is likely to dramatically increase the number of shipments subject to review by border inspectors. Moreover, the varieties of drugs being imported will likely increase so that any given package may contain both prohibited and permitted drugs. Therefore, border inspectors will have to make substantially more difficult judgments than those required under FDA's personal importation policy.

BIO believes these operational complexities will prevent the agencies from effectively implementing any restrictions intended to limit the scope of drug products eligible for importation under any system other than the current requirements of the FDCA, as amended by the Prescription Drug Marketing Act (PDMA).

IMPACT ON PHARMACEUTICAL DISTRIBUTION SYSTEM

II. Assess the pharmaceutical distribution chain and the need for, and feasibility of, modifications in order to assure the safety of imported products.

Should legal importation be limited to wholesale shipments, rather than a much higher volume of small individual drug shipments?

BIO's response:

6/ *Id.*

The FDA's current personal importation policy poses significant challenges to the agencies charged with assuring the safety of imported drug products. The volume and variety of drugs entering the United States that violate federal and state laws continue to climb. FDA and CBP have repeatedly stated that they are unable to inspect the vast quantity of imported mail and express consignment packages that enter the U.S. containing drugs for personal use. If personal importation continues, the volume of such shipments will grow --resulting in uncertified, unlicensed, or unregistered facilities from around the world shipping drug products directly into the U.S. market.

BIO is concerned that consumers lack the knowledge and tools required to assess the attributes of these drug much less their manufacturers, distributors, sellers, shippers, country of origin, or the regulatory oversight they might have received overseas. Consumers will not be adequately protected under any regulatory scheme that permits importation where these factors are unknown or uncontrolled.

Would additional requirements for drug pedigree and "track and trace" records be useful in assisting FDA and other Federal and state agencies to assure the security of these drug imports, i.e., to prevent the introduction of drug products from illegitimate sources? What other mechanisms would be required to enable tracking these products to ensure compliance with applicable considerations or restrictions that are put on them as a result of U.S. law or regulations?

BIO response:

FDA already has the authority to implement a robust drug pedigree system that would assist substantially in controlling illegal diversion and would decrease drug counterfeiting in the U.S. Therefore, BIO strongly encourages the Task Force to recommend and FDA to implement final regulations published in 1989 requiring wholesalers to maintain a pedigree for prescription drugs as mandated by the Prescription Drug Marketing Act of 1987 (PDMA).7/ The PDMA sought to ensure greater accountability for the movement of prescription drugs between licensed and unlicensed prescription drug wholesalers and to prevent the introduction of counterfeit drugs via uncontrolled secondary and tertiary wholesale markets.8/ However, since 2000, FDA has delayed implementing the pedigree requirement. Over approximately the same time frame, the number of FDA

7/ *See* 64 FR 67720 (Dec. 3, 1989).

8/ *Id.* at 67761-62.

counterfeit drug investigations has increased four-fold. 9/ BIO is very concerned that opening the U.S. borders to prescription drug importation will also open an avenue for many more counterfeit drug products. A robust drug pedigree system protects against more than counterfeit drugs – it also helps in assuring that lawful prescription drugs are properly handled and stored during distribution and are not commingled with illegal products. One has to recognize the limits of the pedigree law since it would only apply to products manufactured in the U.S. for U.S. consumption.

Alternatively, any certified drug importation program must at a minimum require:

- the use of authentication and track and trace technology to ensure that imported products are in fact what they purport to be, that they are the product of the declared manufacturer, and that they have not been distributed through multiple countries before export to the U.S.;
- every person handling imported product be licensed and subject to routine mandatory FDA inspections and audits to assure that health and safety regulations are followed including quality assurance testing of each product;
- licensed distributors to immediately report to FDA any counterfeit drugs they encounter, irrespective of whether the drug is destined for the U.S. market or another market;
- all prescription drugs imported under the program be physically held at the first U.S. port of arrival until such time as FDA inspects and releases them into commerce;
- each shipment be filed as a formal CBP entry to ensure adequate control of the entry;
- each entry be covered by a single entry bond sufficient to cover a CBP claim for liquidated damages equal to the article's domestic retail value should the bond principal fail to comply with a bond condition; and
- the importer of record that posts a bond for any drug shipments be based in the United States.

Although these recommendations may assist in controlling the flow of drugs under a certified scheme, they will not be effective if the volume of personal

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9/ *See* Statement of William K. Hubbard, FDA Associate Commissioner for Policy and Planning before the Subcommittee on Healthcare and the Subcommittee on International Trade, Senate Committee on Finance, at http://www.fda.gov/ola/2004/importeddrugs0427.html. (April 27, 2004) ("FDA has seen its number of counterfeit drug investigations increase four-fold since the late 1990s.")

shipments through international mail or express consignment couriers is permitted to increase.

III. Determine the extent to which foreign health agencies are willing and able to ensure the safety of drugs being exported from their countries to the U.S.

BIO response:

BIO does not believe that any foreign country can adequately protect U.S. consumers from adulterated, misbranded, or unapproved imported drugs. Reliance upon foreign regulatory requirements to supplant or replace the assurances of our domestic system of drug approval and regulation would be unprecedented. The FDA is an important participant in extensive global efforts through the International Conference on Harmonisation (ICH) to minimize unnecessary duplicate testing during the research and development of new drugs and to develop guidance documents that create consistency in the requirements for new drug approval. Yet even the ICH is not intended in any way to permit or facilitate the substitution of compliance with one nation's regulatory requirements for another nation's regulatory requirements.

Many American consumers attempt to import drugs from Canada because they believe that Canadian law will protect them from such products. But, nothing in the MMA will assure U.S. consumers that drugs exported from Canada are the same as drugs in Canadian commerce intended for Canadian consumers.

This concern arises from two basic premises of international trade. First, most countries including Canada exercise little or no regulatory oversight to goods *leaving* the country. Therefore, no Canadian law requires that drugs which are not in Canadian domestic commerce meet certain health and safety standards before they may be lawfully exported. Second, goods may move in international commerce and be held in certain countries including Canada without formally entering those countries. Under the trade laws, bonded warehouses may hold goods that are in international commerce but that have not formally been imported under the laws of that country. As a result, goods may flow through Canada and be exported to the United States without ever being subject to Canadian law. As a result, it would be inappropriate for the Secretary to rely on Canadian regulations or laws – or the regulations or laws of any other country – to protect U.S. citizens from adulterated, misbranded, or counterfeit drug products.

A further explanation of bonded warehouses is instructive. Canadian law permits a shipper or importer to bring foreign-made goods into Canadian Customs bonded warehouses in Canada as long as the goods are not intended for

sale in Canada. Moreover, Canada's Food and Drug Act and regulations only apply to drugs that are imported "for sale" in Canada.10/ Therefore, drugs imported into warehouses in Canada may be entirely outside of Health Canada's authority unless or until they enter through Canadian Customs for commercial consumption in the domestic commerce of Canada.

In May 2003, Canada's Health Products and Food Branch addressed this issue. It issued a guidance document concerning import and export of certain drugs. The document applied Canada's drug GMP requirements to drugs "imported into Canada for *commercial purposes*."11/ On May 1, 2004, Health Canada issued another guidance document regarding unapproved drugs imported for packaging or labeling and subsequently exported to a foreign company. As long as the foreign company retains title to the drugs while they are physically packaged or labeled in Canada by a Canadian establishment, "such drugs **are not** sold in Canada."12/

Private companies operate bonded warehouses and routinely lease space to carriers, shippers, distributors, importers, and exporters. Thus, drugs unapproved by Health Canada may be shipped to a Canadian bonded warehouse for repackaging, sorting, and labeling – just the types of activities internet pharmacies and drug distributors are likely to engage in – then be exported to the United States yet never fall under the scope of Canadian law. This creates chain of custody problems because it will be very difficult to trace the drug's ownership. Therefore, the fact that drugs may be exported from Canada can provide no assurance that the drug has ever received regulatory approval or oversight from the Canadian government or its laws.

BIO believes that the scenario described above is the rule rather than the exception and that other countries similarly exercise very limited oversight to drug products being exported to other countries. Therefore, BIO urges that any certified importation scheme expressly prohibit drugs that are transshipped through third party countries before they are exported to the U.S. Implementation of this scheme may pose some important challenges and may require an important commitment of resources by the administration.

10/ *See* R.S. c. F-27 s. 30.

11/ *See* Guidance Document on the Commercial Importation and Exportation of Drugs in Dosage Forms Under the *Food and Drugs Act*, at http://www.hc-sc.gc.ca/hpfb-dgpsa/inspectorate/guide_comm_import_e.pdf (May 1, 2003).

12/ Conditions for Provision of Packaging/Labeling Services for Drugs Under Foreign Ownership (GUIDE-067), at http://www.hc-sc.gc.ca/hpfb-dgpsa/inspectorate/gui_0067_e.pdf (May 1, 2004), at 3 (emphasis in original).

ADEQUACY OF SAFETY PROTECTIONS AND RESOURCES

IV. Identify the limitations, including limitations in resources and in current legal authorities that may inhibit the Secretary's ability to certify the safety of imported drugs.

What impact would restricting importation to products *manufactured* in certain countries (e.g., U.S.) have on adequately regulating those products? How would limitations on importations relating to products *shipped from* certain countries, certain entities within countries, and/or certain ports of entry affect the ability to assure drug safety?

See response to III above.

V. Estimate agency resources, including additional field personnel, needed to adequately inspect the current amount of pharmaceuticals entering the country.

BIO offers no response to this question. However, BIO anticipates and hopes that the U.S. government will provide significant additional resources to the FDA and the CBP to ensure the integrity and safety of the drug supply.

VI. Identify ways in which importation could violate U.S. and international intellectual property rights and describe the additional legal protections and agency resources that would be needed to protect those rights.

BIO's response:

Illegal drug importation directly undermines U.S. intellectual property and contract rights. It seriously and negatively impacts innovative efforts and investment in the pharmaceutical industry. Pharmaceutical and biotechnology innovators spend significant capital on research and development of new therapies with the expectation that U.S. patents will protect their efforts and investments. These are valid and enforceable intellectual property rights under U.S. law.

Drug importation undermines the ability of patent holders to enforce patents through infringement actions. Under current law, the importation of unapproved drugs that purport to be the same as an FDA-approved patented drug infringes valid and enforceable U.S. patents. 13/ Such imports also constitute an

13/ 35 U.S.C. § 271(a).

unfair trade practice. 14/ Drug importation will directly undercut the ability to obtain and enforce a general exclusion order from the International Trade Commission for such practices.

Furthermore, drug importation allows parallel trade in prescription pharmaceuticals. Federal law currently prohibits the unauthorized use of a registered trademark when such use is likely to cause confusion or mistake, or to deceive. 15/ Drug products that are manufactured to comply with foreign regulatory requirements often do not comply with FDA requirements. Therefore, foreign shippers of imported drugs that promote their sales through the unauthorized use of registered trademarks are likely to cause confusion among patients, pharmacists, and physicians as to the bioequivalence or approval status of the imported drugs – potentially violating the Lanham Act. Thus, any drug importation that permits parallel trade in branded prescription drugs weakens a registered trademark holder's ability to enforce its intellectual property right and substantially devalues that right.

Finally, many biotechnology and pharmaceutical companies license portions of their rights to other companies. For example, a company might license rights to sell a particular product overseas and retain the U.S. rights. When the European version is imported, the value of that license decreases.

All of these rights are currently being undermined through illegal importation and will be substantially undercut if importation is sanctioned by the U.S. government. Such a program will directly undermine the basic business model underpinning the drug and biotechnology industries, from drug discovery to drug dispensing. The result will be harm to U.S. pharmaceutical and biotechnology innovation and reduced and delayed patient access to innovative and necessary new drugs and biologics.

ROLE OF NEW TECHNOLOGIES

VII. Estimate the costs borne by entities within the distribution chain to utilize anti-counterfeiting technologies that may be required to provide import security.

14/ 19 U.S.C. § 1337(a)(1)(B)(i).

15/ 15 U.S.C. § 1114(1).

We refer the Task Force to the report recently published by the Congressional Budget Office ("CBO"). CBO estimates that the savings from even a broad, multiple-country importation proposal would at most be modest. The cost of technologies, which should be required to ensure authenticity of drugs imported under a certified program, would further reduce these savings.16 Additionally, it is not reasonable or equitable to require manufacturers to bear the costs of new requirements or technologies under any proposal to expand drug importation beyond the current requirements of the FDCA, as amended by PDMA, when the resulting importation activities would be undertaken by entities other than the manufacturers.

LIABILITIES, OTHER COSTS, AND IMPACTS ON INNOVATION

VIII. Assess the potential short- and long-term impacts on drug prices and prices for consumers associated with importing drugs from other countries.

BIO offers no response to this question.

IX. Assess the impact on drug research and development, and the associated impact on consumers and patients, if importation were permitted.

What would be the impact on research and development of drugs and the associated impact on consumers and patients, if changes in importation laws were to be implemented?

BIO response:

Please see our answer to section VI above.

X. Identify The Liability Protections, If Any, That Should Be In Place If Importation Is Permitted For Entities Within The Pharmaceutical Distribution Chain.

BIO response:

BIO believes that any drug importation scheme (including current, illegal importation) complicates the movement of drugs from manufacturer to consumer. This will provide increased opportunities for mishandling, improper storage, mix-ups, and the commingling of legitimate drugs with adulterated,

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16/ *See* Congressional Budget Office, *Would Prescription Drug Importation Reduce U.S. Drug Spending?* CBO Economic and Budget Issue Brief at 6, ftp://ftp.cbo.gov/54xx/doc5406/04-29-PrescriptionDrugs.pdf. (Apr. 29, 2004).

unapproved, and counterfeit drug products. Unlike the current requirements for importation under the FDCA, as amended by PDMA, such a scheme could exponentially increase the chances that the use of imported drugs would be adverse to the public health due to circumstances and conduct entirely beyond the control of manufacturers.

Patients who are harmed by an imported drug will likely seek compensation from the manufacturer. In recent years, there have been an increasing number of lawsuits filed as a result of the distribution and sale of counterfeit pharmaceuticals within the United States. If a drug importation scheme is put in place, manufacturers will need increased protection from these types of lawsuits because importation and re-importation increase the risk that counterfeit product will find a way into the chain of distribution, and it will be virtually impossible for buyers and FDA to track the chain of distribution of counterfeit products that have entered the U.S.

Incidents of drug counterfeiting are on the rise. A recent article in the New England Journal of Medicine states, "The number of investigations of possible counterfeit drugs by the Food and Drug Administration has jumped from 5 per year in the 1990s to more than 20 per year since 2000."17/ Counterfeiters are especially drawn to high-cost drugs and biologics, particularly expensive injectables. 18/

In addition, counterfeiters have become increasingly sophisticated. Former FDA Commissioner, Mark McClellan, recently noted that drug counterfeiters now have access to state-of-the-art production equipment including modern punch tools and dyes. Thus, counterfeiters have largely shifted their activities toward producing finished products – imitations of popular, high-value pharmaceuticals. Counterfeiting of finished products is even more difficult for investigators to detect.

While counterfeiting is increasingly problematic in the United States, less than one percent of drugs in the U.S. are believed to be counterfeit. These numbers are dramatically higher overseas. "Reports from Asia, Africa and South America indicate that 10 to 50 percent of prescription drugs in certain countries may be counterfeit. In India, the number of counterfeit drugs is so high that the Indian parliament is expected to pass a bill authorizing the death penalty for drug

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17 Paul M. Rudolf & Ilisa B.G. Berstein, "Counterfeit Drugs," *N. England J. Med* 350:14 at 1385.

18 See National Specified List of Susceptible Products issued by the National Association of Boards of Pharmacy and available at http://www.nabp.net.

counterfeiters."19 Similarly, "according to [the] FDA, up to 40% of the Mexican-made pharmaceutical supply is counterfeit."20 Thus, opening the U.S. pharmaceutical market to importation and re-importation will increase the risk that counterfeits will enter the chain of distribution in the U.S.

If it is difficult to track and locate counterfeit product now, it will be almost impossible to do so when drugs are coming into the U.S. from Canada and overseas. A buyer today has a difficult time tracing a chain of distribution that includes transactions made on the basis of a handshake and deals cut in backrooms. That same buyer will face exponentially increased difficulties when the chain of distribution goes through foreign countries and sellers who may not speak English at all let alone keep the type of records necessary to ensure that product is genuine. Current U.S. laws and regulations are not working to eliminate counterfeiting in the U.S. The same laws and regulations will be even less successful in eliminating foreign counterfeiting practices.

The FDA has authority to investigate suspected or reported incidents of counterfeiting within the United States. For example, last year the FDA worked with state officials in Florida to locate and arrest three people for trafficking and unlawfully distributing counterfeit prescription drugs.21 But the FDA does not have the same authority to make investigations outside of the United States.

The number of lawsuits filed against the manufacturers of products counterfeited by others has risen sharply in recent years. Legal protection from liability is necessary for product manufacturers who cannot rely on the power of the U.S. government to identify and punish foreign counterfeiters.

ROLE OF NEW TECHNOLOGIES

XI. Analyze whether anti-counterfeiting technologies could improve the safety of products in the domestic market as well as those products that may be imported.

BIO's response:

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19 Rudolf & Berstein, supra at 1385; see also Lew Kontnik, "Counterfeits: The Cost of Combat," *Pharmaceutical Executive* (Nov. 2003) at 47.

20 Bette Hileman, "Counterfeit Drugs," *Chemical & Eng. News* (Nov. 10, 2003) at 36.

21 Counterfeit Drugs Questions & Answers at http://www.fda.gov/oc/initiatives/counterfeit/qa.html

Several Task Force questions address the potential to use new technologies to combat counterfeiting and mitigate security risks associated with drug importation. FDA's Counterfeit Drug Task Force Final Report discussed the potential benefits of such technologies. 22/

BIO has serious concerns that the application of certain proposed technological solutions for authenticating products, or tracking and tracing them through the distribution cycle, could result in adulteration or degradation of therapeutic proteins and parenteral drugs. For instance, many biological products are highly sensitive to impurities in any quantity. The introduction of very small quantities of a seemingly benign substance as a marker could cause protein aggregation or an immunogenic response. Because of these types of product sensitivities, it would be unwise for the Task Force to recommend the use of covert markers and taggants for use with biological products. Moreover, many "active" technologies (*e.g.,* radio frequency identification or electromagnetic identification systems) require multiple screenings to track the progress of a product through its distribution cycle. It is unknown to what extent repeated exposure to electromagnetic radiation could cause degradation of biological products. Therefore, technologies that require electromagnetic radiation emission must be adequately validated before use with biological products.

BIO agrees with the FDA Counterfeit Drug Task Force Report that a multi-layered approach to drug product security, that incorporates a combination of technological, business, and marketing solutions, could be helpful in combating counterfeiting or product tampering. Regardless, the simplest and most direct tool against these harms is regulatory control over the drug distribution system. Drug importation destroys this control – one that has effectively protected patients for decades.

Conclusion

BIO appreciates the efforts the Task Force members have made to solicit input from all interested stakeholders and we appreciate the opportunity to participate in this process. Opening U.S. borders to importation and reimportation of pharmaceuticals and biologicals would supplant FDA's high standard for quality, safety, and effectiveness. This policy would stifle innovation and damage U.S. intellectual property and contract rights for minimal savings to the health care

22/ *See Combating Counterfeit Drugs: A Report of the Food and Drug Administration,* at http://www.fda.gov/oc/initiatives/counterfeit/report02_04.html (Feb. 2004).

system and to individual consumers. For these reasons, we request that the Task Force urge the Secretary to refuse to certify or support any drug importation program.

We look forward to continuing to work closely with the Secretary and FDA on these important issues.

Sincerely,

/s/

Carl Feldbaum
President, Biotechnology Industry Organization